1st AP

Applicant: Wang et al
Serial No.: 09/767,538
Filed: January 23, 2001
For: ARRAYS FOR BRINGING TWO OR MORE REAGENTS IN CONTACT WITH ONE OR MORE BIOLOGICAL TARGETS AND METHODS FOR MAKING AND USING THE ARRAYS
Group: 1639

Commissioner of Patents and Trademarks
P.O. Box 1450
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Introductory Remark

This is a Response to the Office Communication dated Oct 30, 2008 in the subject application. This document is an amended Appeal Brief for the subject application. It presents no new claim amendments.

The Office Communication dated Oct 30, 2008 states that "Applicants mistakenly identify sections in the specification where support is allegedly found, and are not reasonably specific for the supported limitations. For Example, in the specification as originally filed, none of the pages have paragraph numbers. Even so, page 5 of the specification does not appear to the 50th paragraph as alleged by Applications at page 4 of the Supplement Appeal Brief filed on July 23, 2008".

In response, the Applicant has amended the Appeal Brief accordingly.

Real Party in Interest

The inventors, Yingjian Wang and Yingyi Wang, who reside at 100 Barber Avenue, Worcester, MA 01606.

Related Appeals and Interferences

A pre-Appeal Brief was filed on September 25, 2006. There are no other prior or pending appeals, interferences or judicial proceedings which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision.

Status of Claims

Of all the claims, 37-39, 43-46, 49 and 53 are rejected. Claims 47-48 are canceled. Claims 1-36, 40-42 and 50-52 are withdrawn from consideration.

Claims 37-39, 43-46, 49 and 53 are being appealed.

Status of Amendments

There is no additional amendment filed subsequent to final rejection of the Office Action on May 24, 2006.

Summary of Claimed Subject Matter

The claimed method provides novel arrays of biological reagents and methods of using the arrays to introduce multiple biological reagents into target cells. Each reagent is introduced into a specific subset of cells at a pre-defined position. In the method, a plurality of biological reagents are first arrayed and immobilized on an array support in a defined order; then the array of biological reagents is contacted with the target cells which are immobilized on a second support. Application of a certain condition to the cells (e.g. electric pulse) results in that one or more of the reagents is introduced into a subset of target cells at a unique defined position.

Claim 37 (previously presented): A method for bringing two or more reagents in contact with one or more biological targets comprising the steps of,

providing an array comprising,

two or more reagents; and

one or more barriers adapted to at least temporarily maintain said reagents in at least one arrangement of two or more reagent portions so that said portions do not commingle with each other, wherein each said portion is maintained at a predefined locale in said arrangement so that each of said portions is adapted to be brought into contact with one or more predefined, biological targets;

providing one or more said biological targets on a cell growth support;

designating an address to each reagent portion based on said predefined locale and an address to each of said biological targets;

corresponding at least one of said reagent portions to at least one of said biological targets based on said designated reagent portion and biological target addresses;

contacting said predefined reagent portions with their respective corresponding biological targets;

applying one or more conditions to one or more of said reagent portions to facilitate said transfer of some or all of each specific reagent portion to said specific reagent portion's corresponding biological target, whereby some or all of each specific reagent portion dissociates from said barriers and is transferred to said specific reagent portion's corresponding biological target immobilized on said cell growth support.

Claim 37 embodies an instance of the invention. The arrays and the methods of preparing the arrays are described in the Specification (see page 18 line 8 to page 24, line 9; also see page 25 line 12 to page 26, line 2 for important properties of the arrays that can be used in the method of Claim 37).

Biological targets on a cell growth support are described in the Specification (page 26, line 3 to page 27, line 2; and page 28, line 6 to line 16).

Contacting of reagent portions with their respective corresponding biological targets is described in several places of the Specification, including page 27, line 3 to line 16, and Example 3, page 31, line 6 to line 13.

The step of applying one or more conditions of Claim 37 is described in the Specification (page 27, line 22 to page 28, line 5; and page 28, line 17 to line 20 and Example 3, page 31, line 6 to line 13).

Claim 38 (original): The method of claim 37, wherein said array comprises at least two or more reagents and wherein at least one of said reagent portions comprises all or part of two or more reagents.

The method of Claim 38 uses arrays containing two or more reagents (described throughout the Specification).

Claim 39 (original): The method of claim 37, wherein one or more of said reagents is selected from a group consisting of DNA, RNA, antibodies, peptides, proteins, enzymes, carbohydrates, oligonucleotides, recombinant vectors, drugs, viruses, bacteria, mammalian cells, small organic molecules, and large organic molecules.

The method of Claim 39 uses reagents selected from DNA, RNA, antibodies, peptides, proteins, enzymes, carbohydrates, oligonucleotides, recombinant vectors, drugs, viruses, bacteria, mammalian cells, small organic molecules, and large organic molecules (see Specification, page 18 line 16 to page 19 line 6).

Claim 43 (original): The method of claim 37, wherein said barriers comprise one or more supports having at least one substantially level surface comprising a plurality of spaces surrounding and between said reagent portions wherein said reagent portions are maintained at said predefined locations so that said portions do not commingle.

The method of Claim 43 uses support of leveled surface (see Specification, page17 line 23 to page 24, line 9).

Claim 44 (original): The method of claim 43, wherein one or more of said supports comprises one or more solid supports selected from a group consisting of rigid glass plates, rigid plastic plates, nitrocellulose membranes, nylon membranes, polyvinylidene difluoride membranes, metal membranes, and porous membranes.

The method of Claim 44 uses support made of rigid glass plates, rigid plastic plates, nitrocellulose membranes, nylon membranes, polyvinylidene difluoride membranes, metal membranes, and porous membranes (see Specification, page 23 line 16 to page 24 line 3).

Claim 45 (original): The method of claim 43, wherein one or more of said supports comprises a layer of one or more polymers adapted to immobilize one or more of said reagents.

The method of Claim 45 uses supports of polymers to immobilize reagents (see Specification, page 23 line 16 to page 24 line 3).

Claim 46 (previously presented): The method of claim 37, wherein said step of providing one or more biological targets comprises the step of seeding and adhering two or more cells on said cell growth support.

The method of Claim 46 uses cells seeded on a cell growth support. For description, please see Specification, page 26 line 3 to page 27 line 21.

Claim 49 (previously presented): The method of claim 37, wherein said step of applying one or more conditions comprises the step of applying one or more electric pulses to one or more of said reagent portions.

The method of Claim 49 uses electric pulses to transfect reagents into cells (see Specification, page 28 lines 6-16 and Example 3, page 31, line 6 to line 13.

Claim 53 (previously presented): The method of claim 37, further comprising the step of separating said cell growth support from said array.

The method of Claim 53 further includes the step of separating cell growth support form reagent arrays (see Specification, page 28 line 21 to page 29 line 2).

Grounds of Rejection to be Reviewed on Appeal.

In the Office Action dated May 24, 2006 Claims 37-39, 43-46 and 53 are rejected under 35USC 102(e) as being anticipated by Moynihan et al., US Pat. No. 6,365,349 B1.

The Office Action states *"Claim is directed to a method of bringing two or more reagents into contact with one or more biological targets, comprising an array of reagents contacting a group of biological targets on cell growth support, wherein the reagents locations are addressed.*

Moynihan teaches an improved pipette dispenser for use in biological assays in array format. Moynihan teaches that her invention is relevant to the combinatorial arts for the testing of many samples (i.e., two or more reagents)...

Moynihan discloses a well-known apparatus in the art for dispensing the reagents to the array for delivery the two or more reagents...

Moynihan, col. 3, lines 1-13 (emphasis added). The pipette comprise "barriers" as claimed by Applicants, as Applicants' claims are open to the physical geometries of the barriers."

Claims 37, 43-46, 49 and 53-55 are also rejected under 35 U.S.C. 103 (a) as being unpatentable over Balch, US Pat. 6,083,763 in view of Moynihan et al., US Pat. No. 6,365,349 B1.

The Office action states *"Balch teaches a method and apparatus for analyzing molecular structures within a sample substance using an array having a plurality of test sites upon which the sample substance is applied...*

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Balch and Moynihan teach laboratory based assays via the use of automated, array-based fluid deposition apparatus..."

Argument

The Applicant respectfully appeals the Examiner's current rejections and offers the following arguments.

Arguments against the rejection under 35USC 102(e)

In the Office Action dated May 24, 2006 Claims 37-39, 43-46 and 53 are rejected under 35USC 102(e) as being anticipated by Moynihan et al., US Pat. No. 6,365,349 B1.

In rejecting the claims, the Office Action states "*Claim is directed to a method of bringing two or more reagents into contact with one or more biological targets, comprising an array of reagents contacting a group of biological targets on cell growth support, wherein the reagents locations are addressed.*

Moynihan teaches an improved pipette dispenser for use in biological assays in array format. Moynihan teaches that her invention is relevant to the combinatorial arts for the testing of many samples (i.e., two or more reagents)...

Moynihan discloses a well-known apparatus in the art for dispensing the reagents to the array for delivery the two or more reagents...

Moynihan, col. 3, lines 1-13 (emphasis added). The pipette comprise "barriers" as claimed by Applicants, as Applicants' claims are open to the physical geometries of the barriers."

In response, the Applicant respectfully traverses the Examiner's conclusion and offers the following remarks.

1). Although what Moynihan et al. teaches is relevant to the arts for testing many samples, the reference does not teach the method of Claim 37. Specifically, Moynihan et al. does not teach the steps of: a). providing an array and providing cells on a separate cell growth support, b). applying one or more conditions to one or more of said reagent portions to facilitate said transfer of some or all of each specific reagent portion to said specific reagent portion's corresponding biological target, c).dissociation of reagent from said barriers and is transferred to said specific reagent portion's corresponding biological target immobilized on said cell growth support. The reference does not teach the step of separating said cell growth support from said array (as the method of Claim 53 does) either.

2). The method of Moynihan et al. teaches an improved pipette dispenser for making arrays and use of the arrays in biological assays. However, the arrays of Moynihan and their usage are very different from the arrays of Claim 37.

In the method of Moynihan the arrays are incubated with targets that are provided in a solution mixture, whereby, the targets are captured on the arrays. In contrast, in the method of Claim 37, the reagent array on an array support is contacted with targets on a cell growth support, whereby, the reagents dissociate from the support and transferred into the cells.

3). The emphasis added by the Office Action in the citation of Moynihan only resembles some elements of the claimed method but not the method itself.

For example, the emphasis of "*In the fields of molecular biology and microbiology it has long been common in the art to make replicate arrays of biological agents to facilitate parallel*

testing of many samples" just states that parallel testing is commonly practiced in the fields. There are many different parallel testing methods and the present invention is a new one.

The emphasis of "*Likewise, 96-well mictotiter plates have long been used to store, in an organized and easily accessed fashion, large number of cell lines and virus isolates representing recombinant DNA libraries or monoclonal antibody cell lines.*" bears no relevance to the claimed methods except that cell lines may be used.

4). The method of cell culture as taught by Moynihan can not be used in the method of Claim 37. In the method of Moynihan cells are seeded on solid support (e.g. 96-well microtiter plates) and generally they can not be used in the method of Claim 37. Only cells seeded on a cell support in specific ways can be used in the method of Claim 37 (see the instant Application, page 26 line 3 to page 28 line 16).

5). Similar rejections were raised in previous Office Action and were overcome.

In rejecting Claim 37, the Office Action dated April 23, 2004 states *that "Claims 37-39, 43-45, and 47-48 were rejected under 35 U.S.C. §102(e) as anticipated by Chin et al. (U.S. Patent No. 6,197,599, issued 3/01, filed 7/98)... Chin et al. teach both a method and apparatus for making micro arrays comprising 'two or more reagents' (e.g. 2 or more polynucleotides or polypeptides) and 'one or more barriers...wherein each portion is maintained at predefined positions...portions is adapted to be brought into contact with one or more predefined biological targets' in which the 'barrier' comprises a 'solid support' (e.g. uncoated or glass coated with a polymer i.e. polylysine and grids e.g. addresses)...."*

Although the references used are different (the current rejection was over Moynihan while the rejection in the Office Action dated April 23, 2004 was over Chin et al.), the main reasons are identical: the reference teaches the use of reagent arrays.

The reason for rejecting Claim 37 was also described in the Office Action dated May 03, 2005. Specifically, Claims 37, 43-46 and 53-55 are rejected under 35 USC 102 as being anticipated by Palsson US Pat. 5,811,274. In rejecting the instant claims, The Office Action states that *"Palsson teaches a method of contacting 2 or more reagents with 1 or more biological targets comprising: a. providing an array or 2 or more reagents (e.g. "particles"; see col. 4 and patent claims) on a coated (e.g. polylysine) or uncoated "support" (e.g. cell growth support: see col. 5, especially lines 38- including membranes i.e. porous)... b. providing 1 or more biological targets 9e.g. eukaryotic cells: see col. 5) for contacting the reagent array in which the "biological targets' can be "localized" for contacting and/or immobilized (e.g. attached) to a support (e.g. see col. 3, especially lines 30-40); c and d.. applying 1 or more "conditions" to promote contact, dissociation and transfer (e.g. transfection) (e.g. see bottom of col. 7-col. 8) of the particle DNA into the cell(s) into the corresponding target cell(s). See also example and patent claims".*

In both cases, the rejections were overcome.

Arguments against the rejection under 35USC103(a)

Claims 37, 43-46, 49 and 53-55 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Balch, US Pat. 6,083,763 in view of Moynihan et al., US Pat. No. 6,365,349 B1.

In rejecting the claims, the Office Action states *"Balch teaches a method and apparatus for analyzing molecular structures within a sample substance using an array having a plurality of test sites upon which the sample substance is applied...*

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Balch and Moynihan teach laboratory based assays via the use of automated, array-based fluid deposition apparatus..."

In response, the Applicant respectfully traverses the Examiner's conclusion and offers the following remarks.

1). The method of Balch reference teaches specific methods of constructing arrays and methods of analyzing multiple analytes. However, the methods are very different from the method of Claim 37. Several elements of the Claim 37 are not taught in any of the embodiment of the reference.

First, the method of Balch did not comprise the step of providing an array as well as biological targets on a cell growth support.

Second, the method of Balch did not teach the step of contacting reagent array on an array support with targets on a cell growth support. In the methods of Balch the targets (different from the reagents immobilized on an array) are provided as a mixture and no address is designated for each of the targets (see Balch column 10, line 52 to column 11, line 26).

Third, the method of Balch did not teach the step of applying conditions to facilitate transfer of reagent to target. The method of Claim 37 includes the step of dissociation of reagent

from the array support. In contrast, Balch teaches the method of binding of ligand targets onto the array. It does not teach a method for bringing two or more reagents in contact with one or more biological targets in which at least a portion of the reagents dissociate from the array to the target.

2). In rejecting Claim 49, the Office Action *states "One of the embodiments of the method/apparatus, relates to any array of dispensing units, wherein electric pulses are used to dispense reagents from array to the substrate (col. 11, lines 33-54); as in claim 49".*

The Applicant respectfully disagrees with this statement. In the reference, including col. 11, lines 33-54, electric pulses are used to dispense reagents from a reservoir onto a substrate to produce reagent arrays ("Biosite Deposition").

In contrast, the method of Claim 37 uses electric pulses to transfect cells (but not making arrays). As described in the Specification (page 28 lines 6-20) electric pulses have two effects: help the release of the reagents from the array and help the entrance of the reagents into the cells.

3). The Office Action states "*One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Balch and Moynihan teach laboratory based assays via the use of automated, array-based fluid deposition apparatus".*

As argued above, both Balch and Moynihan references teach the method of arraying reagents. Neither teaches the use of reagent arrays to transfect cells as the instant Claim 37. The use of the arrays in the references does not include transfection and not all types of arrays can be

used in transfection. In fact the arrays described in the references are not suitable for cell transfection. They are used in assays to capture ligands from a solution mixture.

4). The Office Action further states *"One of ordinary skill in the art would have been motivated to extend the application of Balch's apparatus to cell-based assays because of their importance in the art, such as drug discovery as taught by Moynihan. Accordingly, the invention as a whole was prima facie obvious at the time it was invented."*

The applicant respectfully disagrees with this statement. Although both Balch and Moynihan teach methods and apparatus using array format and Moynihan teaches growth of cells in 96-well microtiter plates, neither reference suggests the use of arrays of regents with cells growing on a support. Balch teaches the method of making arrays, however, it did not suggest using his arrays with cells on a support. It did not suggest transfecting the reagents from the arrays into cells either.

Moynihan teaches cell culture but did not teach at all to use the method of making and using arrays for transfecting cells. Therefore, neither method suggest the combination of using reagent arrays and cells to transfect the reagents into cells in a positional addressable manner, as in the method of Claim 37. On of ordinary skill in the art would not have the motivation to extend Balch's arrays to cell-based assays for the purpose of introducing reagents into cells (i.e. transfection).

Even a person in the art applies Balch's apparatus to the cell-based assays as taught by Moynihan, it will not result in the method of Claim 37. This is due to several reasons. First, Balch does nut suggest that reagents can dissociate from his arrays. In fact, Balch uses his arrays to capture ligands onto the array support. Dissociation of reagents from his arrays would be

undesirable in his method. Second, Moynihan et al. did not teach seeding cells on supports that are suitable for transfecting cells. As described in the present invention (e.g. Specification, page 26 ine 10 to page 27, line 2; and page 28, line 6 to line 16), suitable supports may have certain properties, e.g. porous or electrically conducting. Therefore, the use of reagent arrays of Balch's with cells on the support, e.g. 96-well plates, as taught by Moynihan, will not result in the transfection of the reagent into cells in a position-addressable manner (as the method of Claim 37).

Respectfully submitted,

Yingjian Wang, Ph.D.

November 28, 2008

Appendix of Appeal Brief

Claims Appendix

Claim 1 (withdrawn): An array for bringing one or more reagents in contact with two or more biological targets comprising,

one or more reagents; and

one or more barriers adapted to at least temporarily maintain said reagents in at least one arrangement of two or more reagent portions so that said portions do not commingle with each other, wherein each said portion is maintained at a predefined locale in said arrangement so that each of said portions is adapted to be brought into contact with one or more predefined, biological targets.

Claim 2 (withdrawn): The array of claim 1, comprising at least two or more reagents wherein at least one of said reagent portions comprises all or part of two or more reagents.

Claim 3 (withdrawn): The array of claim 1, wherein one or more of said reagents is selected from a group consisting of DNA, RNA, antibodies, peptides, proteins, enzymes, carbohydrates, oligonucleotides, recombinant vectors, drugs, viruses, bacteria, mammalian cells, small organic molecules, and large organic molecules.

Claim 4 (withdrawn): The array of claim 1, wherein one or more of said barriers comprises one or more at least partial capillary tubes.

Claim 5 (withdrawn): The array of claim 4, wherein one or more of said capillary tubes is made of at least one material selected from a group consisting of plastic, glass, nitrocellulose, nitrobenzyloxymethyl cellulose, aminobenzlyoxymethyl cellulose, aminophenylthioether cellulose, diethylaminoethyl cellulose, and polyvinylidene flouride.

Claim 6 (withdrawn): The array of claim 4, wherein said capillary tubes have diameters between 1μm to 1cm.

Claim 7 (withdrawn): The array of claim 4, wherein one or more of said arrangements comprises between 10 to 100,000 capillary tubes.

Claim 8 (withdrawn): The array of claim 4, wherein said capillary tubes have diameters between 1μm to 1cm.

Claim 9 (withdrawn): The array of claim 4, wherein one or more of said arrangements comprises between 100 to 10,000 capillary tubes.

Claim 10 (withdrawn): The array of claim 4, wherein one or more of said arrangements comprises a cross-sectional slice of a plurality of said capillary tubes.

Claim 11 (withdrawn): The array of claim 10, wherein said capillary tubes of said cross-sectional slice have a height between about 1μm to 1cm.

Claim 12 (withdrawn): The array of claim 10, wherein said capillary tubes of said cross-sectional slice have a height between about 10μm to 1cm.

Claim 13 (withdrawn): The array of claim 1, wherein one or more of said reagents are immobilized among said barriers using one or more carriers comprising one or more components selected from a group consisting of cellulose, carbolynmethylcellulose, agarose, dextran, polyaminopolystyrene, polylysine, ploy acrylamides, and derivatives thereof.

Claim 14 (withdrawn): The array of claim 1, wherein two or more of said reagent portions are adapted to be brought simultaneously into contact with two or more predefined, biological targets.

Claim 15 (withdrawn): The array of claim 1, wherein one or more of said reagent portions are adapted to transfect one or more of said reagents into one or more predefined, biological targets.

Claim 16 (withdrawn): The array of claim 1, wherein one or more of said reagent portions is adapted to stain one or more predefined, biological targets.

Claim 17 (withdrawn): The array of claim 1, wherein one or more of said barriers comprises one or more supports having at least one substantially level surface comprising a plurality of spaces surrounding and between said reagent portions wherein said reagent portions are maintained at said predefined locations so that said portions do not comingle.

Claim 18 (withdrawn): The array of claim 17, wherein one or more of said supports is made of at least one material selected from a group consisting of plastic, glass, nitrocellulose, nylon, polyvinylidene fluouride, and metal.

Claim 19 (withdrawn): The array of claim 17, wherein one or more of said supports comprises one or more solid supports selected from a group consisting of rigid glass plates, rigid plastic plates, nitrocellulose membranes, nylon membranes, polyvinylidene difluoride membranes, metal membranes, and porous membranes.

Claim 20 (withdrawn): The array of claim 17, wherein one or more of said supports comprise a layer of one or more polymers adapted to immobilize one or more of said reagents.

Claim 21 (withdrawn): The array of claim 20, wherein one or more of said polymers are selected from a group consisting of polylysine and polyethyleneimine.

Claim 22 (withdrawn): A method for making one or more arrays for bringing one or more reagents in contact with two or more biological targets comprising the steps of,

providing one or more reagents; and

providing one or more barriers adapted to at least temporarily maintain said reagents in at least one arrangement of two or more reagent portions;

immobilizing said reagent portions in said arrangement so that said portions do not comingle with each other, whereby each said portion is maintained at a predefined locale in said arrangement so that each of said portions is adapted to be brought into contact with one or more predefined, biological targets.

Claim 23 (withdrawn): The method of claim 22, wherein one or more of said barriers comprises one or more at least partial capillary tubes, and wherein said step of immobilizing comprises the steps of,

introducing one or more of said reagents into said capillary tubes; and

bundling said capillary tubes in said predefined arrangement.

Claim 24 (withdrawn): The method of claim 23, further comprising the step of cutting said bundled capillary tubes into a plurality of cross-sectional slices.

Claim 25 (withdrawn): The method of claim 23, wherein said step of introducing comprises the steps of, mixing one or more of said reagents with one or more carrier solutions; placing said mixture of reagents and carrier solution into one or more of said capillary tubes; at least partially solidifying said mixture until said mixture is substantially immobile.

Claim 26 (withdrawn): The method of claim 25, further comprising the step of cutting said bundled capillary tubes into a plurality of cross-sectional slices.

Claim 27 (withdrawn): The method of claim 23, wherein one or more of said capillary tubes is made of at least one material selected from a group consisting of plastic, glass, nitrocellulose, nitrobenzyloxymethyl cellulose, aminobenyloxymethyl cellulose, aminophenylthioether cellulose, diethylaminoethyl cellulose, and polyvinylidene fluoride.

Claim 28 (withdrawn): The method of claim 23, wherein one or more of said arrangements comprises between 10 and 100,000 capillary tubes.

Claim 29 (withdrawn): The method of claim 23, wherein one or more of said arrangements comprises at least 10,000 capillary tubes.

Claim 30 (withdrawn): The method of claim 22, wherein one or more of said reagents are immobilized among said barriers using one or more carriers comprising one or more components selected from a group consisting of cellulose, carbolynmethylcellulose, agarose, dextran, polyaminopolystyrene, polylysine, polyacrylamides, and derivatives thereof.

Claim 31 (withdrawn): The method of claim 23, further comprising the steps of removing said reagent portions from said tubes and fixing said portion to one or more supports having one or more substantially level surfaces wherein said reagent portions are maintained at said predefined locations so that said portions do not commingle.

Claim 32 (withdrawn): The method of claim 31, wherein said step of immobilizing further comprises the steps of,

pretreating one or more of said surfaces by applying one or more layers of one or more polymers, adapted to interact with one or more of said reagents.

Claim 33 (withdrawn): The method of claim 32, wherein one or more of said polymers is selected from a group consisting of polylysine and polyethyleneimine.

Claim 34 (withdrawn): The method of claim 31, wherein one or more of said supports is made of at least one material selected from a group consisting of plastic, glass, nitrocellulose, nylon, polyvinylidene fluoride, and metal.

Claim 35 (withdrawn): The method of claim 31, wherein one or more of said supports comprises one or more solid supports selected from a group consisting of rigid glass plates, rigid plastic plates, nitrocellulose membranes, nylon membranes, polyvinylidene difluoride membranes, metal membranes, and porous membranes.

Claim 36 (withdrawn): The method of claim 22, wherein one or more of said reagents is selected from a group consisting of DNA, RNA, antibodies, peptides, proteins, enzymes, carbohydrates, oligonucleotides, recombinant vectors, drugs, viruses, bacteria, mammalian cells, small organic molecules, and large organic molecules.

Claim 37 (currently amended): A method for bringing two or more reagents in contact with one or more biological targets comprising the steps of,

providing an array comprising,

two or more reagents; and

one or more barriers adapted to at least temporarily maintain said reagents in at least one arrangement of two or more reagent portions so that said portions do not commingle with each other, wherein each said portion is maintained at a predefined locale in said arrangement so that each of said portions is adapted to be brought into contact with one or more predefined, biological targets;

providing one or more said biological targets on a ~~target~~ cell growth support;

designating an address to each reagent portion based on said predefined locale and an address to each of said biological targets;

corresponding at least one of said reagent portions to at least one of said biological targets based on said designated reagent portion and biological target addresses;

contacting said predefined reagent portions with their respective corresponding biological targets;

applying one or more conditions to one or more of said reagent portions to facilitate said transfer of some or all of each specific reagent portion to said specific reagent portion's corresponding biological target, whereby some or all of each specific reagent portion dissociates from said barriers and is transferred to said specific reagent portion's corresponding biological target immobilized on said ~~target~~ cell growth support.

Claim 38 (original): The method of claim 37, wherein said array comprises at least two or more reagents and wherein at least one of said reagent portions comprises all or part of two or more reagents.

Claim 39 (original): The method of claim 37, wherein one or more of said reagents is selected from a group consisting of DNA, RNA, antibodies, peptides, proteins, enzymes, carbohydrates, oligonucleotides, recombinant vectors, drugs, viruses, bacteria, mammalian cells, small organic molecules, and large organic molecules.

Claim 40 (withdrawn): The method of claim 37, wherein one or more of said barriers comprise one or more at least partial capillary tubes.

Claim 41 (withdrawn): The method of claim 40, wherein said barriers comprise a plurality of bundled capillary tubes.

Claim 42 (withdrawn): The method of claim 41, wherein said barriers comprise a plurality of bundled capillary tubes.

Claim 43 (original): The method of claim 37, wherein said barriers comprise one or more supports having at least one substantially level surface comprising a plurality of spaces

surrounding and between said reagent portions wherein said reagent portions are maintained at said predefined locations so that said portions do not commingle.

Claim 44 (original): The method of claim 43, wherein one or more of said supports comprises one or more solid supports selected from a group consisting of rigid glass plates, rigid plastic plates, nitrocellulose membranes, nylon membranes, polyvinylidene difluoride membranes, metal membranes, and porous membranes.

Claim 45 (original): The method of claim 43, wherein one or more of said supports comprises a layer of one or more polymers adapted to immobilize one or more of said reagents.

Claim 46 (currently amended): The method of claim 37, wherein said step of providing one or more biological targets comprises the step of seeding and adhering two or more cells on said ~~target~~ cell growth support.

Claim 47 (cancelled): The method of claim 37, wherein said step of contacting said predefined reagent portions with their respective corresponding biological targets, whereby some or all of each specific reagent portion is transferred to said specific reagent portion's corresponding biological target, comprises the step of, seeding and adhering one or more of said biological targets on said biological targets' corresponding predefined reagent portions.

Claim 48 (cancelled): The method of claim 37, wherein said step of contacting step comprises the step of applying one or more conditions to one or more of said reagent portions to facilitate said transfer of some or all of each specific reagent portion to said specific reagent portion's corresponding biological target.

Claim 49 (previously presented): The method of claim 37, wherein said step of applying one or more conditions comprises the step of applying one or more electric pulses to one or more of said reagent portions.

Claim 50 (withdrawn): A method for bringing one or more reagents in contact with two or more biological targets comprising the steps of,

providing an array comprising,

two or more reagents; and

one or more barriers adapted to at least temporarily maintain said reagents in at least one arrangement of two or more reagent portions so that said portions do not comingle with each other, wherein each said portion is maintained at a predefined locale in said arrangement so that each of said portions is adapted to be brought into contact with one or more predefined, biological targets;

providing one or more biological targets;

designating an address to each reagent portion based on said predefined locale and an address to each of said biological targets;

corresponding at least one of said reagent portions to at least one of said biological targets based on said designated reagent portion and biological target addresses;

contacting said predefined reagent portions with their respective corresponding biological targets, whereby some or all of each specific reagent portion is transferred to said target's corresponding specific reagent portion.

Claim 51 (withdrawn): The method of claim 37, wherein one or more of said barriers comprises one or more capillary tubes.

Claim 52 (withdrawn): The method of claim 51, wherein said barriers compromise one or more cross-sectional slices of said capillary tubes.

Claim 53 (currently amended): The method of claim 37, further comprising the step of separating said ~~target~~ cell growth support from said array.

Claim 54 (canceled): A method for bringing two or more reagents in contact with one or more biological targets comprising the steps of,

providing an array comprising two or more reagents; and one or more barriers adapted to at least temporarily maintain said reagents in at least one arrangement of two or more reagent portions so that said portions do not commingle with each other, wherein each said portion is maintained at a predefined locale in said arrangement so that each of said portions is adapted to be brought into contact with one or more predefined, biological targets;

providing one or more biological targets on said array, wherein at least one of said reagent portions contacts at least one of said biological targets;

applying one or more conditions, whereby some or all of each specific reagent portion dissociates from said array and is transferred to said specific reagent portion's corresponding biological target.

Claim 55 (canceled): The method of claim 54, wherein said biological targets are eukaryotic cells.

Claim 56 (canceled): The method of claim 54, wherein said step of applying one or more conditions comprises the step of applying one or more electric pulses to one or more of said reagent portions.

Evidence Appendix

None.

Related Proceedings Appendix

None.